REMARKS

This Amendment is in response to the third non-final Office Action mailed November 10, 2008 (the Action). Claims 1-26 and 51 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,014,214 to Li (Li) in view of U.S. Patent No. 6,725,073 to Motamedi et al (Motamedi) and U.S. Patent No. 7,039,452 to McClane (McClane).

Applicants have rewritten Claim 23 in independent form, and therefore, the above amendments are fully supported by the Specification as originally filed. Applicants respectfully request reconsideration for the following reasons.

I. Independent Claim 1

Claim 1 recites as follows:

> A non-invasive *in vivo* method for assessing carotenoids in the retina and/or macula, comprising:
> performing Optical Coherence Tomography (OCT) on a retina of a subject; and
> generating a spatial representation of carotenoid levels in the retina based on data from the OCT of the retina.

Applicants submit that none of the cited references disclose or render obvious generating a spatial representation of *carotenoid levels* in the retina based on *data from the OCT of the retina* as recited in Claim 1.

Li discusses using low coherence light (*i.e.*, polychromatic) sources to perform OCT. *See* col. 1, lines 12-20 (cited in the Action). The Action concedes that Li does not use OCT for the purpose of measuring the concentration of a substance in tissue, but states that Motamedi teaches methods for measuring "analyte concentration" in a tissue using OCT. *See* the Action, page 2 (citing Motamedi, Abstract). The Action notes that "Motamedi specifically mentions glucose as one analyte of interest." Although the Action concedes that Li and Motamedi do not teach measuring carotenoid levels in the retina, the Action apparently takes the position that the OCT techniques of Motamedi could be applied to "any substance." The Action then cites McClane as assessing a risk of age-related macular degeneration by measuring carotenoid levels using Raman imaging, and concludes that it

would have been obvious to "modify Li/Motamedi, to measure the concentration of carotenoids in the retina as taught by McClane." *See* the Action, page 3.

Applicants respectfully disagree with the Action's conclusion because 1) the OCT techniques of Motamedi cannot be applied to detect "any substance" such as carotenoid levels because Motamedi relies on specific characteristics of glucose not shared by carotenoids that change tissue scattering, and 2) combining the polychromatic OCT techniques of Li and Motamedi would destroy the stated purpose of the monochromatic Raman imaging techniques of McClane to detect carotenoid levels.

Motamedi relies on very specific characteristics of glucose to calculate glucose concentration using low coherent light sources in OCT. Motamedi states as follows (emphasis added):

> Embodiments described herein take advantage of glucose's ability to decrease tissue scattering. Further, the embodiments described herein also <u>take advantage of glucose's ability to alter optical and morphological characteristics of tissue, body fluids, or implants</u>. Such optical properties include, but are not limited to, scattering, reduced scattering, anisotropic factors, absorption coefficients, indices of refraction, and any other measurable optical characteristic....It appears that <u>the ability of glucose to decrease tissue scattering is based, at least in part, on its properties as an osmolyte</u> - properties known in the art. Changes in tissue scattering due to <u>refractive index changes are more specifically attributed to glucose as an osmolyte than changes in tissue absorption spectra due to the presence of glucose as a chromophore</u>...

See col. 6, lines 21-50.

In summary, Motamedi states that OCT uses the detection of photons coherently scattered from tissue (*see* col. 6,lines 2-3) to detect <u>glucose concentrations</u> by taking advantage of "<u>glucose's ability to alter optical and morphological characteristics of tissue, body fluids, or implants</u>." *See* Col. 6, lines 23-25. Motemedi specifically attributes the scattering changes to glucose's properties as an <u>osmolyte</u>. An osmolyte is a compound that affects osmosis by playing a role in cell volume and fluid balance.

Applicants submit that <u>carotenoids are not osmolytes</u>, and therefore, there is no reasonable expectation of success that the techniques of Motamedi could be applied to "any

substance," and in particular, to non-osmolyte carotenoids. As noted above, Motamedi specifically states that glucose concentrations can be detected due to the ability of glucose to alter optical and morphological characteristics of tissue because of its its status as an osmolyte. Applicants cannot locate any portion of Motamedi that discusses any other analytes other than glucose, and carotenoids are not even osmolytes.

As stated in the MPEP 2141, when considering obviousness of a combination of elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (emphasis added)(citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007)). Thus, applying the OCT techniques of Motamedi's glucose concentration measurements (which are purported to take advantage of specific characteristics of glucose as an osmolyte) on another "analyte" such as carotenoids (which is not an osmolyte) as proposed by the Action is not a predictable use of prior art elements according to their established functions. Thus, Applicants submit that the rejections under 35 U.S.C. 103(a) cannot stand.

Moreover, McClane does not cure the deficiencies of Li and Motamedi because applying the polychromatic OCT techniques in Li and/or Motamed would destroy the stated purpose of monochromatic Raman imaging techniques of McClane. As noted in Applicants' papers of February 17, 2008 and October 6, 2008, McClane uses monochromatic light to generate a Raman signal. Specifically, McClane discusses that "the invention comprises obtaining a light source that generates light at a wavelength that produces a Raman response with a wavelength shift for one or more macular carotenoids." *See* McClane, col. 5, lines 3-6. The scattered light includes inelastically scattered light having a plurality of Raman signals corresponding to one or more macular carotenoids. The elastically scattered light is filtered out and the inelastically scattered light is analyzed. *See* McClane, col. 5, lines 6-14. The light source in McClane is further described as a device for generating "nearly monochromatic light" at a wavelength that overlaps the absorption bands of the carotenoids of interest. *See* McClane, col. 5, lines 30-36. In contrast, conventional OCT (such as is discussed in Li and Motamedi) uses polychromatic light to generate an OCT scan. The polychromatic light sources of Li and Motamedi would destroy the purpose of McClane,

which uses monochromatic light generated at a wavelength that produces a Raman response in carotenoids. Thus, applying the polychromatic light sources of Li and Motamedi to McClane would appear to render the Raman excitation wavelengths discussed in McClane inoperable.

For at least the reasons discussed above, Applicants submit that Claim 1 is patentable over Li, Motamedi and McClane. Claims 2-22, 26 and 51 depend from Claim 1 and are likewise patentable. In addition, Applicants submit that at least certain dependent claims are separately patentable for at least the following reasons.

II. Dependent Claims

Dependent Claims 2-22, 26 and 51 are patentable at least for the reasons discussed with respect to Claim 1. In addition, at least certain dependent claims are separately patentable for the following reasons.

It is noted that the Action provides no discussion of any recitations of dependent Claims 2-22, 26 and 51. In particular, Applicants cannot locate any disclosure in the references for at least the following recitations of the dependent claims.

- performing OCT includes transmitting a blue excitation light to the retina (Claim 2)
- performing OCT includes transmitting an excitation light including a blue excitation light and an infrared excitation light (Claim 3)
- the generating step includes applying a wavelet transformation to an OCT signal to generate spectral data of the retina (Claim 4)
- transmitting a low coherent light with a super luminescent diode (Claim 5)
- repeating the performing and generating steps after administration of a selected treatment to provide a first and second spatial representation of carotenoids levels in the retina (Claim 7) and comparing the first spatial representation with the second spatial representation and evaluating the efficacy of the selected treatment on age-related macular degeneration (AMD) based on comparing step (Claim 8)
- comparing a detected light spectrum from the OCT to *a priori* reference spectra corresponding to a plurality of known concentrations of the carotenoids (Claim 11)

- detecting a resonant Raman spectra based on the OCT data (Claim 13)
- generating a two-dimensional map of carotenoids levels in a cross-sectional spatial representation of the retina from the OCT (Claim 17)

Applicants submit that Li, Motemedi and McClane do not disclose or render obvious at least the above-emphasized recitations of the dependent claims. Such claims are therefore separately patentable, and Applicants respectfully request an indication of same. However, if the rejections are maintained, Applicants respectfully request that the specific portions of the references that are alleged to disclose the recitations of the dependent claims be identified in any subsequent Office Action.

III. <u>Claims 23-25</u>

As noted above, Claim 23 has been rewritten in independent form. Claims 24-25 depend from Claim 23. Accordingly, Claims 23-25 include the recitations of Claim 1 and are patentable at least for the reasons discussed above. Applicants submit that Claims 23-25 are also patentable for at least the following additional reasons.

In addition to the recitations of Claim 1, Claim 23 recites as follows (emphasis added):

> illuminating a portion of the retina with an optical excitation beam having a wavelength selected to generate a resonant Raman spectrum of at least one of the carotenoids;
>
> detecting a resonant Raman spectrum corresponding to the selected illuminated region of the eye; and
>
> <u>combining resonant Raman spectrum data with OCT data</u> to generate the spatial representation of carotenoid levels in the retina.

As discussed above, Li and Motemedi use polychromatic OCT to examine biological tissues. McClane use monochromatic Raman spectroscopy to detect carotenoids. None of the cited references disclose or render obvious at least <u>combining resonant Raman spectrum data with OCT data</u> to generate the spatial representation of carotenoid levels the retina as recited in Claim 23.

Claim 24 depends from Claim 23 and recites that the generating and illuminating steps are performed substantially simultaneously. Applicants submit that this recitation is also not disclosed or rendered obvious from the cited references.

Claim 25 depends from Claim 24 and recites that the generating step further includes detecting an OCT signal, and the method further includes <u>filtering the resonant Raman spectrum from the OCT signal</u>. As noted above, Li, Motemedi and McClane do not discuss combining resonant Raman spectrum data with OCT data, and therefore, Li, Motemedi and McClane also do not disclose filtering at the resonant Raman spectrum from the OCT signal as recited in Claim 25.

Accordingly, Applicants submit that Claims 23-25 are patentable over the cited prior art in request that the rejections be withdrawn.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

Respectfully submitted,

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CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on <u>February 10, 2009.</u>

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Joyce Paoli